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published in
Asian Pacific Journal of Cancer Prevention
2012

DOI (link to publisher)
10.7314/APJCP.2012.13.12.6491

document version
Publisher's PDF, also known as Version of record

RESEARCH ARTICLE

Socio-economic Status Plays Important Role in Childhood Cancer Treatment Outcome in Indonesia

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Abstract

Background: The influence of parental socio-economic status on childhood cancer treatment outcome in low-income countries has not been sufficiently investigated. Our study examined this influence and explored parental experiences during cancer treatment of their children in an Indonesian academic hospital. Materials and Methods: Medical charts of 145 children diagnosed with cancer between 1999 and 2009 were reviewed retrospectively. From October 2011 until January 2012, 40 caretakers were interviewed using semi-structured questionnaires. Results: Of all patients, 48% abandoned treatment, 34% experienced death, 9% had progressive/relapsed disease, and 9% overall event-free survival. Prosperous patients had better treatment outcome than poor patients (P<0.0001). Odds-ratio for treatment abandonment was 3.3 (95%CI: 1.4-8.1, p=0.006) for poor versus prosperous patients. Parents often believed that their child's health was beyond doctor control and determined by luck, fate or God (55%). Causes of cancer were thought to be destiny (35%) or God's punishment (23%). Alternative treatment could (18%) or might (50%) cure cancer. Most parents (95%) would like more information about cancer and treatment. More contact with doctors was desired (98%). Income decreased during treatment (55%). Parents lost employment (48% fathers, 10% mothers), most of whom stated this loss was caused by their child's cancer (84% fathers, 100% mothers). Loss of income led to financial difficulties (63%) and debts (55%). Conclusions: Treatment abandonment was most important reason for treatment failure. Treatment outcome was determined by parental socio-economic status. Childhood cancer survival could improve if financial constraints and provision of information and guidance are better addressed.

Keywords: Childhood cancer - socio-economic status - adherence - low-income country - Indonesia

Asian Pacific J Cancer Prev, **13 (12)**, 6491-6496

Introduction

The cure rate of childhood cancer may be as high as 80% in high-income countries, but frequently is less than 35% in low-income countries (Smith et al., 2010). Poor treatment adherence by health-care providers, parents and patients importantly contributes to this difference in survival. Abandonment of treatment, a severe form of non-adherence, is one of the most common reasons for treatment failure in low-income countries (Arora et al., 2010; Lam et al., 2012)

Recently the SIOP PODC Abandonment of Treatment Working Group declared that treatment abandonment can no longer be ignored by the international pediatric oncology community (Mostert et al., 2011). More insight into underlying causes is needed. Providing access to care, improving treatment adherence and reducing abandonment should be a top priority for those involved in childhood cancer care in low-income countries in order to narrow down the gap between the outcomes of children with cancer in high and low-income countries (Arora et al., 2007; Mostert et al., 2011).

Although it is generally believed that financial difficulties of parents are a major contributor to abandonment of childhood cancer treatment (Bonilla et al., 2009; Sitaresmi et al., 2010), very few studies have actually demonstrated any impact of parental socio-economic status on abandonment and survival of childhood cancer patients in low-income countries. Also in Prof Dr RD Kandou Hospital (KH) in Manado, Indonesia, insight into the role that socio-economic status plays in childhood cancer treatment is missing.

Here we examined the influence of parental socio-economic status on childhood cancer treatment outcome, and parental experiences during cancer treatment of their children at KH. The obtained insights may help to design strategies to improve adherence, reduce abandonment and increase survival rates in low-income countries.

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Materials and Methods

Setting

Indonesia has approximately 245 million inhabitants, 27% (66 million) of whom are children younger than 15 years (CIA, 2012). A childhood cancer incidence of 102 per million children less than 15 years old in low-income countries (Parkin et al., 1988; 1998; Howard et al., 2008), leads to an estimated 6,700 new childhood cancer cases in Indonesia each year.

Our study was conducted at KH in Manado at the island of Sulawesi. This academic hospital is the only centre treating children with cancer in the provinces of Gorontalo, North-Sulawesi, North-Maluku and West-Papua. The estimated population KH hereby serves is 5 million people, including 1.4 million children less than 15 years old. Around 140 childhood cancer patients under 15 are expected in KH's service area.

The pediatric oncology department at KH covers 18 beds and is run by 2 pediatric oncologists and 17 nurses. Three different wards are recognized: first, second and third class. With rising rank, conditions on ward and quality of provided food improve and number of children per hospital room decreases. However, treatment protocols and medical staff are the same for all patients. No information material about cancer and its treatment is available.

Indonesia distinguishes three types of social health-insurance: 1) Askes for civil-servants, 2) Jamsostek for private-sector employees, 3) Jamkesmas for the poor. Jamkesmas was instituted in 2004. Jamkesmas-insured patients do not pay premiums (Rokx et al., 2009). Because health-insurance plans changed several times, it has been unclear which costs were covered.

Children are assigned to a specific hospital ward on basis of parental income and health-insurance. Askes patients are assigned to first or second class, depending on the importance of their parents' position in government. Jamsostek patients are assigned to second class. Jamkesmas patients are automatically assigned to third class.

Study design

This was a combined retrospective medical records study and cross-sectional study with semi-structured questionnaires.

In the medical records study inclusion criteria for all children were newly diagnosed malignancy and age between 0 to 16 years at diagnosis. First presentation of patients occurred between January 1999 and October 2009.

We collected the following variables from medical records: name and registration number of childhood cancer patient, type of cancer, gender, age at first presentation, year of first presentation, assigned hospital class at diagnosis, health-insurance and treatment outcome.

Malignancies were diagnosed by histological examination and leukemias by cytomorphology. Malignancies were classified in 5 groups: 1) hematological tumors, 2) brain tumors, 3) solid tumors, 4) rare tumors, 5) a group "unspecified" which included patients of whom only the originate tissue of malignancy was known, while pathology was lacking.

Treatment outcome was defined as abandonment of treatment, death, progressive or relapsed disease and event-free survival. In line with SIOP recommendations (Mostert et al., 2011), abandonment of treatment was defined as failure to start or continue scheduled curative treatment during 4 or more consecutive weeks.

Parental socio-economic status divided children as coming from poor or prosperous families, based on 2 determinants: 1) Assigned hospital class at diagnosis. Patients attending first and second class were classified as prosperous. Patients attending third class as poor. 2) Health-insurance. Askes and Jamsostek were classified as prosperous, Jamkesmas as poor. Both determinants were obtained routinely during hospital admission and recorded in medical records. In case of discordance between both determinants, assigned hospital class at diagnosis prevailed.

The cross-sectional study consisted of a semi-structured questionnaire. The focus was to assess psychological and socio-economic experiences of parents during cancer therapy. Participants were caretakers of childhood cancer patients who were hospitalized or visited the outpatient clinic at KH between October 2011 and January 2012. Respondents were interviewed by an independent interviewer. The questionnaire contained statements that parents could evaluate on three-point rating scales (agree/uncertain/disagree). A panel of Dutch and Indonesian doctors and psychologists made sure of appropriate, clear and coherent statements. Questionnaire was pilot-tested on a separate group of parents for its content, clarity of language and cultural sensitivities. A few minor adjustments were made on basis of pilot-test. Anonymity and confidentiality were guaranteed. Study was approved by Medical Ethics Committee of KH.

Data analysis

Frequency distributions were calculated. Relationship between treatment results, parental socio-economic status and patient characteristics were evaluated by chi-squared and Fisher's Exact tests. Probability of event-free survival was estimated by Kaplan-Meier method: estimates were compared using log-rank test. Event-free survival was measured from date when patient received diagnosis of cancer to first treatment failure or last follow-up. Data management and analysis were performed with SPSS for Windows version 17.0. Fisher's Exact tests for variables with more than two categories were performed in R version 2.9.1.

Results

Medical record study

In the period January 1999 to October 2009, 145 patients were diagnosed with a malignancy and met study's inclusion criteria. These 145 patients consisted of 76 (52%) boys and 69 (48%) girls. New patients seen in KH for pediatric cancer ranged from 4-28 per annum. Annual average was 15 patients. Ages at admission ranged between 0-15 years. Incidence peak was observed between

3-6 years. Mean age at time of diagnosis was 6.1 years (SD=3.7), median 5.4.

Figure 1 shows distribution of different types of cancer. Of all 145 children, specific diagnosis was confirmed in 132 (91%) patients: hematological tumors (n=105, 80%), solid tumors (n=20, 15%), rare tumors (n=5, 4%) and brain tumors (n=2, 2%). In class of hematological tumors, acute lymphoblastic leukemia was most common (n=71, 68%).

Of 145 children, treatment outcome was not known in 2 patients. These patients had moved and received treatment in another hospital.

Abandonment of treatment was the most common cause of treatment failure (Figure 2). Of 143 patients, 68 (48%) abandoned treatment: 40 (59%) patients refused therapy and 28 (41%) patients initially started treatment and later dropped-out. Table 1 shows reasons of parents for abandoning therapy of their child. It is noteworthy that this information was obtained from medical records, and not from families concerned.

The second most common treatment failure was death. In total, 49 (34%) patients died due to: infection (15), hemorrhage (10), other causes (17), no data (7). Distribution of death was: prior to treatment (28), during treatment (17), after completion of treatment (4).

The least common treatment failure was progressive or relapsed disease, which occurred in 13 (9%) patients: progressive disease (1) and relapse (12). Distribution of progressive or relapsed disease was: during treatment (10), and after completion of treatment (3).

Event-free survival was achieved by 13 (9%) patients: acute lymphoblastic leukemia (11), Hodgkin lymphoma (1) and retinoblastoma (1).

Of 143 patients with documented treatment outcome, 112 patients were classified as poor (78%) and 31 patients as prosperous (22%). No discordance between both determinants of socio-economic status occurred. No significant differences in types of cancer were found between both groups. The most likely treatment outcome in poor patients (n=112) was abandonment of treatment (n=60, 54%), whereas in prosperous patients (n=31) it was both event-free survival and treatment-related death (n=9, 29%). Figure 3 shows significant differences in treatment outcome between poor and prosperous patients (P<0.0001). Odds-ratio for treatment abandonment was 3.3 (95% CI: 1.4-8.1, p=0.006) for poor versus prosperous population.

Of 143 patients with documented treatment outcome, time until event could not be retrieved in 5 charts. Figure 4 shows that event-free survival estimate was significantly higher in prosperous (n=29) than in poor (n=109) patients (P=0.001). Note that Figure 3 shows actual percentages, whereas Kaplan-Meier estimates in Figure 4 show time-dependent probability estimates.

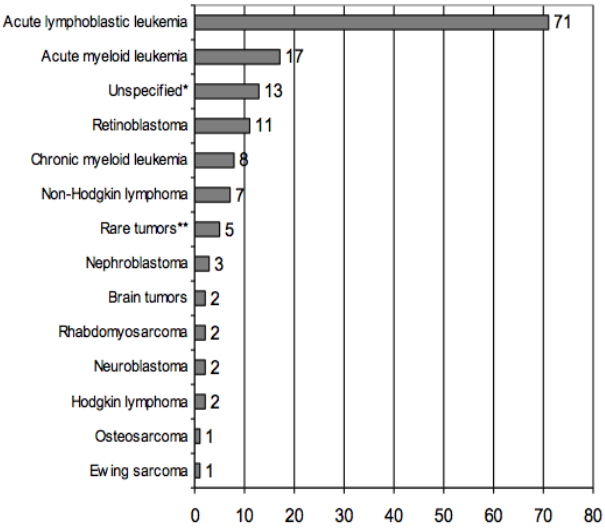

Figure 1. Distribution of Childhood Cancer Types at KH, Manado, Indonesia between 1999-2009 (n=145). *Only the originate tissue of the malignancy was known, e.g." abdominal tumor". **Such as germ cell tumors, follicular thyroid carcinoma, hepatoblastoma

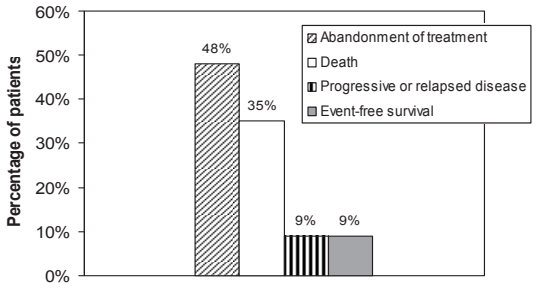

Figure 2. Treatment Outcome in Children with Cancer at KH, Manado, Indonesia (n=143)

Questionnaire study

From October 2011 till January 2012, 41 childhood cancer patients attended KH. Caretakers of 40 children (98%) were interviewed. Parents of 1 child did not participate because their child died before the interview took place. Respondents consisted of 32 (80%) mothers, 5 (13%) fathers, 2 (5%) grandmothers and 1 (3%) sister. The 40 patients consisted of 21 (52%) boys and 19 (48%) girls.

Table 1. Reasons for Treatment Abandonment of 68 Childhood Cancer Patients According to Medical Records

Reasons for abandonment of treatment	N	%
Financial difficulties	29	43
No belief in chemotherapy	14	21
No belief in chemotherapy and financial difficulties	9	13
Refused bone-marrow puncture	8	12
Distance to hospital	4	6
Side-effects of chemotherapy	2	3
Bad condition of child	1	2
No reason recorded	1	2

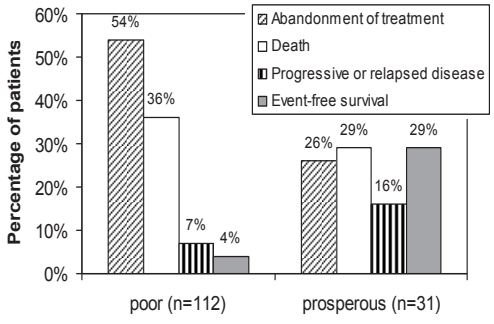

Figure 3. Treatment Outcome Per Parental Socio-economic Status in Children with Cancer at KH, Manado, Indonesia (n=143, P<0.0001)

Patients had hematological tumors (n=36, 90%) or solid tumors (n=4, 10%). Acute lymphoblastic leukemia was by far most common hematological tumor (n=31, 86%). At time of interviewing, 38 children (95%) were still in treatment and 2 children (5%) had completed treatment. According to our socio-economic status classification 35 (88%) children came from a poor and 5 (13%) children from a prosperous background.

Psychological aspects

Beliefs: Cancer can be cured according to 38 parents (95%). Parents believed that health of their child was beyond doctor's control and determined by luck, fate or God (n=22, 55%), and some parents were uncertain of this statement (n=10, 25%). Causes of cancer in their child were thought to be destiny (n=14, 35%), punishment of God (n=9, 23%), bad luck (n=1, 3%), and unknown (n=1, 3%). When their child appeared healthy again, 12 parents (30%) thought their child was cured from cancer, and 14 parents (35%) were uncertain.

Complementary or alternative treatment: Alternative treatment could cure cancer according to 7 parents (18%) and 20 parents (50%) were uncertain about this. Combination of chemotherapy and alternative treatment was the best way to cure cancer according to 14 parents (35%) and 13 (38%) were uncertain. Used complementary or alternative sources of treatment were spiritual or religious help (n=30; 75%), traditional medicine (n=11; 28%), massage (n=10, 25%), physiotherapy (n=4, 10%) and paranormal support (n=1, 3%).

Parental education and communication: Most parents (n=38, 95%) would like to receive more information about cancer and its treatment. More contact with their doctor was desired by 39 parents (98%). When the doctor explained about disease, treatment and medication, 16 parents (40%) found it hard to understand. Eighteen parents (45%) had difficulties with learning or memorizing doctor's statements and advices. Fifteen parents (38%) had difficulties understanding vocabulary of doctors. Parents of other children were used as source of information about cancer by 35 caretakers (88%).

Medication adherence: Table 2 lists reasons for not administering drugs at home. It was easier to remember to give medication to their child after they recently visited hospital according to 36 parents (90%). Difficulties to tell their doctor the truth about how they managed their disease and took prescribed medication were mentioned by 10 parents (25%).

Marital status: Of all parents, 39 (98%) were married and 1 parent (3%) was widowed. Difficulties to understand the way their spouse was responding to all stress were experienced by 17 parents (43%). Fifteen parents (38%) had marital problems due to disease of their child.

Siblings: Of 40 families, 32 (80%) had more than one child. Twenty-three parents (72%) had less time and energy for siblings. Feelings of guilt towards siblings were expressed by 14 parents (44%). Siblings felt neglected according to 13 parents (41%). Seventeen parents (53%) were afraid of the well-being of siblings.

Coping: Impact of cancer on family life increased during course of treatment according to 34 families (85%). Parents were preoccupied with fatal return of cancer (n=25, 63%). Parents described their child's emotional condition as unhappy in 5 cases (13%), and themselves as unhappy in 10 cases (25%). Caretakers were positive about quality of relationship with their child (n=34, 85%). Table 3 shows coping characteristics.

Socio-economic aspects

Parental employment: Parents of 19 children (48%) had regular income per month. Income decreased since start of treatment according to 22 families (55%). During

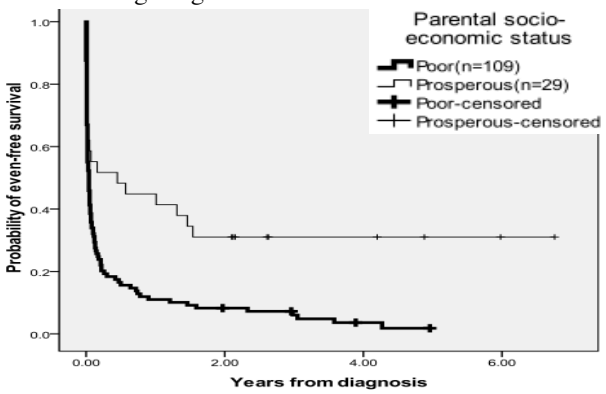

Figure 4. Kaplan-Meier Estimates of Event-free Survival Per Parental Socio-economic Status (P=0.001). Events included abandonment of treatment, death, and progressive or relapsed disease. Heavy solid line, poor(n=109); solid line, prosperous(n=29); heavy plus, poor censored; plus prosperous censored

Table 2. Reasons Parents of 40 Childhood Cancer Patients for Non-adherence with Medication Administration at Home

Reasons for non-adherence medication at home	N	%
Forgetting	15	38
Financial difficulties parents	7	18
Too busy	6	15
Child looks healthy	3	8
Child refuses drugs	3	8
Lack of knowledge of protocol	2	5
Side-effects of chemotherapy	1	3
Inadequate supply of drugs at pharmacy	1	3
Alternative treatment	1	3
Lack of motivation doctors	1	3

Table 3. Coping Characteristics of Parents of 40 Childhood Cancer Patients

Coping characteristics	N	%
Feelings towards illness of their child:		
Hope and optimism	38	95
Worrying	37	93
Acceptance	35	88
Sadness	31	78
Scared	23	58
Depression	12	30
Ashamed	4	10
Most difficulties to cope with disease:		
Mothers	14	35
Fathers	12	30
Patients	7	17
Grandparents	4	10
Siblings	1	2
Aunts	1	2
Both parents	1	2

Table 4. Transportation Characteristics of Parents of 40 Childhood Cancer Patients

Transportation characteristics	N	%
Distance to hospital:		
<30 km	12	30
30-60 km	10	25
>60 km	18	45
Mode of transportation:		
Public transport	32	80
Renting a vehicle	4	10
Private motorbike or car	3	8
Travel time to hospital:		
< 1 hour	14	35
1-3 hours	13	33
> 3 hours	10	25
Perception of transportation:		
Time consuming	25	63
Difficult	22	55
Expensive	21	53

treatment 19 fathers (48%) lost their job, 16 of whom (84%) identified their child's cancer as the cause. In total 4 mothers (10%) lost their jobs, and all (100%) due to disease of their child.

Financial difficulties: Loss of income led to financial difficulties (n=25, 63%) and debts (n=22, 55%). Financial difficulties were perceived as great burden according to 22 parents (55%). Costs of treatment forced 4 parents (10%) to withhold their child of certain aspects of prescribed treatment. Only 5 parents (13%) believed that they would not be able to complete treatment due to financial problems, and 6 (14%) parents were uncertain.

Health-insurance and sponsors: Thirty-eight families (95%) had health-insurance: askes (4), jamkesmas (34). Insurance covered treatment costs completely (n=3, 8%) or partially (n=35, 92%). Other sponsors paying for treatment were: family members (n=31, 78%), religious community (n=23, 58%), friends (n=14, 35%), neighbors (n=12, 30%), village community (n=11, 28%), colleagues (n=6, 15%) and employer (n=4, 10%).

Transportation: Table 4 illustrates transportation characteristics. Distances to clinic, absence of proper transport and transportation costs were never reasons to miss hospital appointments according to consecutively 20 (50%), 21 (53%) and 21 (53%) families.

Discussion

Abandonment of treatment was the most important reason for treatment failure at KH in Manado, Indonesia. Because most abandonment occurs during diagnostic process, efforts to reduce its magnitude should be implemented when patients first enter hospital. Differences in treatment outcome between poor and prosperous patients were sizeable. Abandonment of treatment was significantly more frequent in poor patients. Kaplan-Meier estimate of event-free survival was significantly lower in poor patients.

According to medical records the most important reason for abandonment of treatment was financial difficulties of parents. During interviews with caretakers we indeed found that socio-economic impact of cancer treatment was profound, despite availability of health-insurance. Many parents became unemployed due to illness of their child. Prolonged treatment costs combined with decreased incomes caused most families to experience financial difficulties that resulted in debts. Caretakers indicated that health-insurance covered only a part of medical expenses.

According to medical records another important reason for abandonment of treatment was disbelief in usefulness of chemotherapy. From questionnaires we learned that parents often believed that health of their child was beyond doctor's control and determined by luck, fate or God. Therefore conventional treatment may not be considered sufficient to cure their children (McLean et al., 2006; Hamidah et al., 2009; Al-Qudimat et al., 2011). Spiritual or religious help and traditional medicine were often consulted.

Parents may not believe in effectiveness of conventional cancer treatment because parental education by health-care providers is lacking (Yeh et al., 1999). Almost all parents would have liked to receive more information and attention from their doctor. Many parents have difficulties understanding the information, advices and vocabulary of doctors. As a result, parents may misapprehend the need to complete treatment. Adherence of parents increases if usefulness of treatment and risks of non-adherence are understood (Yeh et al., 1999; Mostert et al., 2010).

In Manado, we also found that beliefs, attitude and behavior of health-care providers differ between poor and prosperous families. Doctors expect poor families to be less adherent and unable to complete treatment. Subsequently less elaborate information, time and attention is given to poor parents (Mostert et al., Submitted). This lack of information may contribute to higher rates of abandonment seen in the poor.

Family life changes dramatically when a child is diagnosed with cancer (Stam et al., 2006). Parents had most difficulties coping with their child's disease and some felt depressed. Parents of other children with cancer were frequently consulted for information and advice. Development of a parent-organization could be beneficial (Naafs-Wilstra et al., 2001).

The referral area of KH suggests that the number of patients with cancer is many times larger than the annual average of 15 patients who visit the pediatric oncology department. Causes in low-income countries are numerous. Lacking awareness of health-issues may delay seeking medical attention. Parents may not recognize symptoms or believe cancer is incurable and medical help futile (Howard et al., 2008; Mostert et al., 2012). Parents may rely on alternative treatment or have no transportation to reach hospital. Families may not afford treatment (Sitaresmi et al., 2010). Health-care providers may not be skilled to recognize childhood cancer. Laboratory and imaging devices may be lacking (Howard et al., 2008). Personnel may believe cancer is incurable or that parents cannot pay treatment and therefore decide referral is not worthwhile (Mostert et al., 2012).

Similarities were found with our previous research on childhood cancer treatment in Yogyakarta, Indonesia (Mostert et al., 2006; 2008). This is all the more

remarkable because Indonesia, the largest archipelago in the world, only became one unified country after gaining independence from Dutch colonial rule in 1949. Differences between Yogyakarta on Java and Manado on Sulawesi are therefore distinct. Distance between them is about 2000 km and both isles have a different history, ethnic population, native language, culture and religion. Inhabitants of Yogyakarta are predominantly Muslim and in Manado Christian (Ricklefs, 2001; CIA, 2012).

Our study has some limitations. Time periods of medical records study and questionnaire study differed. Parents of children who had abandoned treatment were not interviewed. Although the children of the interviewees are still at risk to abandon treatment, this may mean that more adherent caretakers participated in the questionnaire study.

Outcome of childhood cancer treatment could be improved substantially by interventions that help to prevent abandonment of treatment. On the basis of our retrospective and cross-sectional study we recommend the following: 1) Comprehensive parental education at diagnosis about cancer, treatment and necessity of treatment adherence, 2) Follow-up system for detecting and contacting promptly families who miss hospital appointment, 3) Communication training of health-care providers. Health-care providers in low-income countries need to realize that technical know-how is insufficient to cure their patients, 4) Program enabling parents to maintain their income level. Handicraft-programs (Howard et al., 2004; AMPATH, 2012) offering parents work opportunities to cover treatment costs are good examples. 5) Adapt health-insurance so that all necessary medical expenses are covered. These measures most likely will have a positive influence on adherence and treatment outcome of children with cancer in Sulawesi, Indonesia, and many other low-income countries as well.

Acknowledgements

We would like to thank Nancy Jocom, Susanti Lisupindan Palimbong and Irna Chandra for their assistance. Our study was supported by grants from Stichting VUmc Fonds and Dutch Cancer Society.

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